AMERICAN VETERINARY MEDICAL ASSOCIATION
1931 N. MEACHAM ROAD, SUITE 100 • SCHAUMBURG, ILLINOIS, 60173-4360
PHONE (847) 925-8070 • FAX (847) 925-1329 • www.avma.org

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June 30, 2004

Docket No. 2003D-0290
Dockets Management Branch (HFA-305)
5630 Fishers Lane
Rockville, MD 20857

Re: Docket No. 2003D-0290
Guidance for FDA Staff and Industry
Compliance Policy Guides Manual (CPG)
Sec. 608.400
Compounding of Drugs for Use in Animals

Dear Sir or Madam:

On behalf of our nation's veterinarians, the American Veterinary Medical Association (AVMA) wishes to urge *amendment* of CPG 608.400 "Compounding of Drugs for Use in Animals." There are not enough FDA approved drugs to treat the numerous species under the veterinary profession's care. In certain limited circumstances, compounding drugs from *bulk* ingredients for *non-food* animals (e.g., pets, horses, exotic animals) is a necessary part of relieving pain and suffering. Consequently, the CPG should provide regulatory discretion for non-food animals within delineated criteria. It is the AVMA's goal to help describe these medically legitimate circumstances and provide proposed criteria for discretion.

The AVMA believes the policy articulated in FDA Compliance Policy Guide 608.400 was written to facilitate enforcement against the illegal use of bulk ingredients, specifically:

- compounding for food producing animals which is a food safety concern,
- compounding for any animal species that involves mass produced or wholesaled preparations that are not patient-specific rather than customized preparations that are prescribed and compounded for individual patients, and
- compounding for any animal species that creates mimics of commercially available FDA approved products.

These activities undermine the FDA drug approval system, expose many animals to unapproved drugs, and potentially threaten animal and public health. The AVMA readily supports enforcement against such acts.

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However, the CPG has one significant shortcoming. It does not offer regulatory discretion for the limited use of medically necessary preparations compounded from bulk ingredients for non-food animals. These are situations in which the need for such therapy is great and the risk is small. The therapeutic agent is administered under professional supervision and public health and animal safety are not threatened. Although legal compounding can begin only with approved drugs, the AVMA believes it is medically necessary for veterinarians or pharmacists to compound from bulk ingredients in limited circumstances. We recognize the CPG makes some mention of regulatory discretion. Appendix A lists nine bulk drug substances for compounding and subsequent use in animals to which CVM would not ordinarily object. However, Appendix A does not cover many medically necessary situations for non-food animals.

There are two general sets of circumstances in which the AVMA believes compounding from bulk ingredients may be necessary:

- the approved drug is not commercially available, or
- the needed compounded preparation cannot be made from the approved drug.

Otherwise the AVMA believes drugs should be compounded only from approved drugs. Cost is not an appropriate reason for compounding from bulk ingredients, whereas animal health and patient medication compliance are legitimate reasons.

- Approved drugs can be unavailable commercially for several reasons:
  a) The approved drug is temporarily unavailable for reasons such as backorder or interruptions in manufacturing,
  b) The sponsor ceases sale of the approved drug for business (not safety) reasons,
  c) No drug containing the needed ingredient was ever approved (e.g., potassium bromide for the control of seizures),
  d) Withdrawn human drugs whose use in animals presents great benefits and negligible risks to animal and public health (e.g., cisapride for treatment of feline megacolon rather than surgical removal of the entire colon or euthanasia).

- Approved drugs can be inadequate for compounding for several reasons:
  a) The concentration of active ingredient in the approved drug is too low to produce a compounded preparation with the needed concentration in a practical dosing volume or size. The dose of compounded suspensions, capsules, or parenterals must be of a volume or size to be practically administered by mouth or injection, including injection by dart.
  b) Compounding from the approved drug has negative effects on the quality of the preparation.
     1. Sterile injectable drugs and eye drops may contain excipients, particulates, or pyrogens if approved drugs are used for compounding.
     2. Gels, creams, or syrups may be gritty and active ingredients may be unevenly dispersed if approved drugs are used for compounding.
     3. Intravenous injections and preparations administered through ophthalmic palpebral catheters and feeding tubes may have particulate

matter rather than being clear if approved drugs are used for compounding.

c) The approved product may contain an ingredient that the patient cannot tolerate (e.g., beef in allergic individuals).
d) Flavoring cannot mask the objectionable taste of some approved drugs. For example, some patients refuse flavored metronidazole hydrochloride because flavoring does not mask the metallic taste. Instead, tasteless metronidazole benzoate is flavored to enhance palatability. However, it is generally preferable to flavor approved drugs rather than bulk drugs because of the assurances of safety, efficacy, and quality that accompany approved drugs.

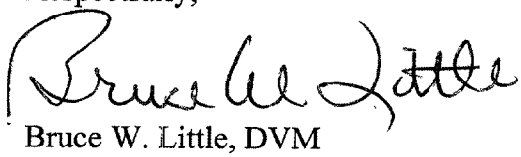
We believe several elements are necessary for the legitimate use of preparations compounded from bulk ingredients:

- ✓ Our requested discretion is limited to non-food animals (i.e., animals not intended for food).
- ✓ Compounding must be only prescription-driven by a licensed veterinarian within a veterinarian-client-patient relationship.
- ✓ Compounded preparations should not be mass-produced or wholesaled for non-specific patient use.
- ✓ Compounded preparations should not mimic commercially available FDA approved drugs.
- ✓ A licensed veterinarian may compound or direct a licensed pharmacist to compound.
- ✓ Drugs should be compounded upon a prescription only for a specific patient or for "in-office use" where allowed by state law.
- ✓ There must be a legitimate medical need for the customized preparation.
- ✓ There must be no approved animal drug or human drug that can adequately treat the condition when either used as labeled, in an extralabel manner, or compounded.
- ✓ Veterinarians and pharmacists should comply with all applicable laws and regulations governing their practice, incorporating regulatory discretion.
- ✓ Bulk ingredients must be purchased from a state registered, if applicable, and FDA registered source that is subject to FDA Good Manufacturing Practices (GMPs) inspections and provides accompanying certificates of analysis for the ingredients.
- ✓ Bulk ingredients must meet or exceed the appropriate compendia standards.
- ✓ Veterinarians and clients should be informed when compounded products are made from bulk ingredients.
- ✓ Pharmacists should provide copies of the certificates of analysis and compendia standards for bulk ingredients to veterinarians upon request.

It is our sincere hope that AVMA has helped distinguish between illegal acts of large scale that may cause harm versus individual, medically legitimate circumstances that would benefit from regulatory discretion. We urge that the FDA CVM amend the CPG

to acknowledge regulatory discretion for veterinarian supervised, legitimate compounding from bulk ingredients that relieves the pain and suffering of non-food animals.

Respectfully,



Bruce W. Little, DVM
Executive Vice President

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